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 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  APR 02  CAS Registry Number Crossover Limits Increased to
                  500,000 in Key STN Databases
 NEWS  3  APR 02  PATDPAFULL: Application and priority number formats
                  enhanced
 NEWS  4  APR 02  DWPI: New display format ALLSTR available
 NEWS  5  APR 02  New Thesaurus Added to Derwent Databases for Smooth
                  Sailing through U.S. Patent Codes
 NEWS  6  APR 02  EMBASE Adds Unique Records from MEDLINE, Expanding
                  Coverage back to 1948
 NEWS  7  APR 07  50,000 World Traditional Medicine (WTM) Patents Now
                  Available in CAplus
 NEWS  8  APR 07  MEDLINE Coverage Is Extended Back to 1947
 NEWS  9  JUN 16  WPI First View (File WPIFV) will no longer be
                  available after July 30, 2010
 NEWS 10  JUN 18  DWPI: New coverage - French Granted Patents
 NEWS 11  JUN 18  CAS and FIZ Karlsruhe announce plans for a new
                  STN platform
 NEWS 12  JUN 18  IPC codes have been added to the INSPEC backfile
                  (1969-2009)
 NEWS 13  JUN 21  Removal of Pre-IPC 8 data fields streamline displays
                  in CA/CAplus, CASREACT,and MARPAT
 NEWS 14  JUN 21  Access an additional 1.8 million records exclusively
                  enhanced with 1.9 million CAS Registry Numbers --
                  EMBASE Classic on STN
 NEWS 15  JUN 28  Introducing "CAS Chemistry Research Report": 40 Years
                  of Biofuel Research Reveal China Now Atop U.S. in
                  Patenting and Commercialization of Bioethanol
 NEWS 16  JUN 29  Enhanced Batch Search Options in DGENE, USGENE,
                  and PCTGEN
 NEWS 17  JUL 19  Enhancement of citation information in INPADOC
                  databases provides new, more efficient competitor
                  analyses
 NEWS 18  JUL 26  CAS coverage of global patent authorities has
                  expanded to 61 with the addition of Costa Rica
 NEWS 19  SEP 15  MEDLINE Cited References provide additional
                  revelant records with no additional searching.
 NEWS 20  OCT 04  Removal of Pre-IPC 8 data fields streamlines
                  displays in USPATFULL, USPAT2, and USPATOLD.
 NEWS 21  OCT 04  Precision of EMBASE searching enhanced with new
                  chemical name field
 NEWS 22  OCT 06  Increase your retrieval consistency with new formats  or
                  for Taiwanese application numbers in CA/CAplus.
 NEWS 23  OCT 21  CA/CAplus kind code changes for Chinese patents
                  increase consistency, save time
 NEWS 24  OCT 22  New version of STN Viewer preserves custom
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                    highlighting of terms when patent documents are
                    saved in .rtf format
 NEWS 25  OCT 28  INPADOCDB/INPAFAMDB: Enhancements to the US national
                    patent classification.
 NEWS 26  NOV 03  New format for Korean patent application numbers in
                    CA/CAplus increases consistency, saves time.
 NEWS 27  NOV 04  Selected STN databases scheduled for removal on
                    December 31, 2010
 NEWS 28  NOV 18  PROUSDDR and SYNTHLINE Scheduled for Removal
                    December 31, 2010 by Request of Prous Science
 NEWS 29  NOV 22  Higher System Limits Increase the Power of STN
                    Substance-Based Searching
 NEWS 30  NOV 22  Enjoy a free month of INPADOCDB/INPAFAMDB SDIs!
 NEWS 31  NOV 24  Search an additional 46,850 records with MEDLINE
                    backfile extension to 1946

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          AND CURRENT DISCOVER FILE IS DATED 07 JULY 2010.

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FILE 'HOME' ENTERED AT 14:50:41 ON 10 DEC 2010

=> fil caplus
COST IN U.S. DOLLARS                                 SINCE FILE      TOTAL
                                                          ENTRY    SESSION
FULL ESTIMATED COST                                        0.22       0.22

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FILE COVERS 1907 - 10 Dec 2010  VOL 153 ISS 25
FILE LAST UPDATED: 9 Dec 2010  (20101209/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Aug 2010
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Aug 2010
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This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s cyclopamine
L1         558 CYCLOPAMINE

=> s cyclopamine/cn
   REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.






L3         277 L2

=> s jervine/cn
   REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.






L5         226 L4

=> fil reg
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.50      16.01

FILE 'REGISTRY' ENTERED AT 14:51:44 ON 10 DEC 2010
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STRUCTURE FILE UPDATES:    9 DEC 2010  HIGHEST RN 1256239-79-8
DICTIONARY FILE UPDATES:   9 DEC 2010  HIGHEST RN 1256239-79-8

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experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> s cyclopamine
L6          10 CYCLOPAMINE

=> s jervine
L7         228 JERVINE

=> fil medline embase biosis
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    11.49      27.50

FILE 'MEDLINE' ENTERED AT 14:52:02 ON 10 DEC 2010

FILE 'EMBASE' ENTERED AT 14:52:02 ON 10 DEC 2010
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FILE 'BIOSIS' ENTERED AT 14:52:02 ON 10 DEC 2010
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=> s l6 or l6<chem> or l7 or l7<chem>

   SmartSELECT INITIATED
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COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     3.33      30.83

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SET SMARTSELECT ON
SET COMMAND COMPLETED

SEL L6 1- CHEM
L8          SEL L6 1- CHEM :      32 TERMS

SET SMARTSELECT OFF
SET COMMAND COMPLETED


COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    15.49      46.32

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FILE 'BIOSIS' ENTERED AT 14:52:17 ON 10 DEC 2010
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S L6 OR L8 OR L7 OR L7<CHEM>

   SmartSELECT INITIATED
New TRANSFER and ANALYZE Commands Now Available
See HELP TRANSFER and HELP ANALYZE for Details


COST IN U.S. DOLLARS                             SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                    3.33      49.65

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SET SMARTSELECT ON
SET COMMAND COMPLETED

SEL L7 1- CHEM
L9          SEL L7 1- CHEM :     387 TERMS

SET SMARTSELECT OFF
SET COMMAND COMPLETED


COST IN U.S. DOLLARS                             SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   15.49      65.14

FILE 'MEDLINE' ENTERED AT 14:52:36 ON 10 DEC 2010

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S L6 OR L8 OR L7 OR L9




L12       7703 L6 OR L10 OR L7 OR L11

=> s l12 and (cancer or tumor or tumour or neoplasm or carcinoma)/ab
L13       1330 L12 AND (CANCER OR TUMOR OR TUMOUR OR NEOPLASM OR CARCINOMA)/AB

=> s l13 and pd<20010702
L14        397 L13 AND PD<20010702

=> s l14 and (cyclopamine or jervine)/ab
L15         12 L14 AND (CYCLOPAMINE OR JERVINE)/AB

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16           5 DUP REM L15 (7 DUPLICATES REMOVED)

=> d l16 1-5 ibib abs
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L16  ANSWER 1 OF 5     MEDLINE on STN                  DUPLICATE 1
ACCESSION NUMBER:    2002074749    MEDLINE
DOCUMENT NUMBER:     PubMed ID: 11748155
TITLE:               The Sonic Hedgehog-Gli pathway regulates dorsal brain
                     growth and tumorigenesis.
AUTHOR:              Dahmane N; Sanchez P; Gitton Y; Palma V; Sun T; Beyna M;
                     Weiner H; Ruiz i Altaba A
CORPORATE SOURCE:    Skirball Institute of Biomolecular Medicine, Developmental
                     Genetics Program and Department of Cell Biology, NYU School
                     of Medicine, 540 First Avenue, New York, NY 10016, USA.
SOURCE:              Development (Cambridge, England), (2001 Dec) Vol.
                     128, No. 24, pp. 5201-12.
                     Journal code: 8701744. ISSN: 0950-1991. L-ISSN: 0950-1991.
PUB. COUNTRY:        England: United Kingdom
DOCUMENT TYPE:       (IN VITRO)
                     Journal; Article; (JOURNAL ARTICLE)
                     (RESEARCH SUPPORT, NON-U.S. GOV'T)
                     (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200202
ENTRY DATE:          Entered STN: 25 Jan 2002
                     Last Updated on STN: 8 Feb 2002
                     Entered Medline: 7 Feb 2002
AB   The mechanisms that regulate the growth of the brain remain unclear.  We
     show that Sonic hedgehog (Shh) is expressed in a layer-specific manner in
     the perinatal mouse neocortex and tectum, whereas the Gli genes, which are
     targets and mediators of SHH signaling, are expressed in proliferative
     zones.  In vitro and in vivo assays show that SHH is a mitogen for
     neocortical and tectal precursors and that it modulates cell proliferation
     in the dorsal brain.  Together with its role in the cerebellum, our
     findings indicate that SHH signaling unexpectedly controls the development
     of the three major dorsal brain structures.  We also show that a variety
     of primary human brain tumors and tumor lines
     consistently express the GLI genes and that cyclopamine, a SHH
     signaling inhibitor, inhibits the proliferation of tumor cells.
     Using the in vivo tadpole assay system, we further show that misexpression
     of GLI1 induces CNS hyperproliferation that depends on the activation of
     endogenous Gli1 function.  SHH-GLI signaling thus modulates normal dorsal
     brain growth by controlling precursor proliferation, an evolutionarily
     important and plastic process that is deregulated in brain tumors
     .

L16  ANSWER 2 OF 5     MEDLINE on STN                  DUPLICATE 2
ACCESSION NUMBER:    2001328790    MEDLINE
DOCUMENT NUMBER:     PubMed ID: 11396162
TITLE:               Inhibitory effect of steroidal alkaloids on drug transport
                     and multidrug resistance in human cancer cells.
AUTHOR:              Lavie Y; Harel-Orbital T; Gaffield W; Liscovitch M
CORPORATE SOURCE:    Department of Biological Regulation, Weizmann Institute of
                     Science, Rehovot 76100, Israel.
SOURCE:              Anticancer research, (2001 Mar-Apr) Vol. 21, No.
                     2A, pp. 1189-94.
                     Journal code: 8102988. ISSN: 0250-7005. L-ISSN: 0250-7005.
PUB. COUNTRY:        Greece
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200107
ENTRY DATE:          Entered STN: 30 Jul 2001
                     Last Updated on STN: 30 Jul 2001
                     Entered Medline: 26 Jul 2001
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AB   Intrinsic or acquired resistance of tumor cells to multiple
     cytotoxic drugs (multidrug resistance MDR) is a major cause of failure of
     cancer chemotherapy.  MDR is often caused by elevated expression
     of drug transporters such as P-glycoprotein (P-gp) or multidrug resistance
     protein (MRP).  A number of compounds, termed chemosensitizers, have
     little or no cytotoxic action of their own, but inhibit (P-gp) or
     MRP-mediated drug export and are capable of sensitizing MDR cells to the
     cytotoxic effects of chemotherapeutic drugs.  Here we examined the ability
     of steroidal alkaloids of plant origin, namely the Veratrum sp. alkaloid
     cyclopamine and the Lycopersicon sp. alkaloid tomatidine, to act
     as potent and effective chemosensitizers in multidrug resistant
     tumor cells.  Drug uptake was determined by measuring accumulation
     of tetramethylrosamine in multidrug resistant NCI AdrR human
     adenocarcinoma cells.  Resistance to adriamycin and vinblastine was
     determined by utilizing the MTT cell survival assay.  Cyclopamine
     and tomatidine elevate tetramethylrosamine uptake by NCI AdrR cells and
     sensitize the cells to the cytotoxic action of adriamycin and vinblastine.
     In both cases these agents are comparable in patency and efficacy to
     verapamil, a reversal agent commonly used in MDR research.  It is
     concluded that steroidal alkaloids of plant origin act as inhibitors of
     P-gp-mediated drug transport and multidrug resistance and therefore may
     serve as chemosensitizers in combination chemotherapy with conventional
     cytotoxic drugs for treating multidrug resistant cancer.

L16  ANSWER 3 OF 5     MEDLINE on STN                    DUPLICATE 3
ACCESSION NUMBER:    2001642041     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 11694189
TITLE:               Acceleration of the formation of cultured epithelium using
                     the sonic hedgehog expressing feeder cells.
AUTHOR:              Kameda T; Hatakeyama S; Terada K; Sugiyama T
CORPORATE SOURCE:    Department of Biochemistry, Akita University School of
                     Medicine, Akita, Japan.. tkameda@med.akita-u.ac.jp
SOURCE:              Tissue engineering, (2001 Oct) Vol. 7, No. 5, pp.
                     545-55.
                     Journal code: 9505538. ISSN: 1076-3279. L-ISSN: 1076-3279.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       (EVALUATION STUDIES)
                     Journal; Article; (JOURNAL ARTICLE)
                     (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200202
ENTRY DATE:          Entered STN: 7 Nov 2001
                     Last Updated on STN: 13 Feb 2002
                     Entered Medline: 12 Feb 2002
AB   Sonic hedgehog (Shh) regulates the principal possesses in many
     developmental stages, including the epithelial-mesenchymal interaction.
     The extraordinary acceleration of signaling by Shh is responsible for the
     development of human basal cell carcinomas and
     trichoepitheliomas; they might originate from the very immature
     keratinocytes, including the stem cells.  We tried to utilize the
     mitogenic effect of Shh to accelerate the formation of cultured
     epithelium, which is already used in the medical field practically.  To
     this end, we transfected shh cDNA into a Swiss-3T3 cell line, widely used
     as a feeder for keratinocytes, and established a Shh expressing cell line.
     The lethally irradiated Shh expressing feeder cells remarkably accelerated
     the growth of keratinocyte colonies obtained from the human neonatal
     foreskin, and the formation of well-stratified cultured epithelium, which
     is rich in immature small keratinocytes, expressing cytokeratin 14.  This
     acceleration was suppressed by the addition of cyclopamine, a
     specific inhibitor of Shh signaling.  These data indicate that the Shh is
     a promising mitogen to improve the technology for cultured epithelium
     formation.

L16  ANSWER 4 OF 5     MEDLINE on STN                   DUPLICATE 4
ACCESSION NUMBER:    2000439367    MEDLINE
DOCUMENT NUMBER:     PubMed ID: 10984056
TITLE:               Effects of oncogenic mutations in Smoothened and Patched
                     can be reversed by cyclopamine.
AUTHOR:              Taipale J; Chen J K; Cooper M K; Wang B; Mann R K;
                     Milenkovic L; Scott M P; Beachy P A
CORPORATE SOURCE:    Department of Molecular Biology and Genetics, Howard Hughes
                     Medical Institute, The Johns Hopkins University School of
                     Medicine, Baltimore, Maryland 21205, USA.
SOURCE:              Nature, (2000 Aug 31) Vol. 406, No. 6799, pp.
                     1005-9.
                     Journal code: 0410462. ISSN: 0028-0836. L-ISSN: 0028-0836.
PUB. COUNTRY:        ENGLAND: United Kingdom
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
                     (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200009
ENTRY DATE:          Entered STN: 28 Sep 2000
                     Last Updated on STN: 28 Sep 2000
                     Entered Medline: 21 Sep 2000
AB   Basal cell carcinoma, medulloblastoma, rhabdomyosarcoma and
     other human tumours are associated with mutations that activate
     the proto-oncogene Smoothened (SMO) or that inactivate the tumour
     suppressor Patched (PTCH).  Smoothened and Patched mediate the cellular
     response to the Hedgehog (Hh) secreted protein signal, and oncogenic
     mutations affecting these proteins cause excess activity of the Hh
     response pathway.  Here we show that the plant-derived teratogen
     cyclopamine, which inhibits the Hh response, is a potential
     'mechanism-based' therapeutic agent for treatment of these tumours
     .  We show that cyclopamine or synthetic derivatives with
     improved potency block activation of the Hh response pathway and abnormal
     cell growth associated with both types of oncogenic mutation.  Our results
     also indicate that cyclopamine may act by influencing the
     balance between active and inactive forms of Smoothened.

L16  ANSWER 5 OF 5     MEDLINE on STN                   DUPLICATE 5
ACCESSION NUMBER:    1999102111    MEDLINE
DOCUMENT NUMBER:     PubMed ID: 9882493
TITLE:               Essential role for Sonic hedgehog during hair follicle
                     morphogenesis.
AUTHOR:              Chiang C; Swan R Z; Grachtchouk M; Bolinger M; Litingtung
                     Y; Robertson E K; Cooper M K; Gaffield W; Westphal H;
                     Beachy P A; Dlugosz A A
CORPORATE SOURCE:    Laboratory of Mammalian Genes and Development, National
                     Institutes of Health, Bethesda, Maryland, 20892, USA.
SOURCE:              Developmental biology, (1999 Jan 1) Vol. 205, No.
                     1, pp. 1-9.
                     Journal code: 0372762. ISSN: 0012-1606. L-ISSN: 0012-1606.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199902
ENTRY DATE:          Entered STN: 23 Feb 1999
                     Last Updated on STN: 23 Feb 1999
                     Entered Medline: 5 Feb 1999
AB   The hair follicle is a source of epithelial stem cells and site of origin
     for several types of skin tumors.  Although it is clear that
     follicles arise by way of a series of inductive tissue interactions,
     identification of the signaling molecules driving this process remains a
     major challenge in skin biology.  In this study we report an obligatory
     role for the secreted morphogen Sonic hedgehog (Shh) during hair follicle
     development.  Hair germs comprising epidermal placodes and associated
     dermal condensates were detected in both control and Shh -/- embryos, but
     progression through subsequent stages of follicle development was blocked
     in mutant skin.  The expression of Gli1 and Ptc1 was reduced in Shh -/-
     dermal condensates and they failed to evolve into hair follicle papillae,
     suggesting that the adjacent mesenchyme is a critical target for
     placode-derived Shh.  Despite the profound inhibition of hair follicle
     morphogenesis, late-stage follicle differentiation markers were detected
     in Shh -/- skin grafts, as well as cultured vibrissa explants treated with
     cyclopamine to block Shh signaling.  Our findings reveal an
     essential role for Shh during hair follicle morphogenesis, where it is
     required for normal advancement beyond the hair germ stage of development.
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=> d his

     (FILE 'HOME' ENTERED AT 14:50:41 ON 10 DEC 2010)

     FILE 'CAPLUS' ENTERED AT 14:50:52 ON 10 DEC 2010
L1          558 S CYCLOPAMINE
                S CYCLOPAMINE/CN

     FILE 'REGISTRY' ENTERED AT 14:51:07 ON 10 DEC 2010
L2            1 S CYCLOPAMINE/CN

     FILE 'CAPLUS' ENTERED AT 14:51:08 ON 10 DEC 2010
L3          277 S L2
                S JERVINE/CN

     FILE 'REGISTRY' ENTERED AT 14:51:34 ON 10 DEC 2010
L4            1 S JERVINE/CN

     FILE 'CAPLUS' ENTERED AT 14:51:34 ON 10 DEC 2010
L5          226 S L4

     FILE 'REGISTRY' ENTERED AT 14:51:44 ON 10 DEC 2010
L6           10 S CYCLOPAMINE
L7          228 S JERVINE

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 14:52:02 ON 10 DEC 2010

     FILE 'REGISTRY' ENTERED AT 14:52:14 ON 10 DEC 2010
                SET SMARTSELECT ON
L8          SEL L6 1- CHEM :      32 TERMS
                SET SMARTSELECT OFF

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 14:52:17 ON 10 DEC 2010

     FILE 'REGISTRY' ENTERED AT 14:52:17 ON 10 DEC 2010
                SET SMARTSELECT ON
L9          SEL L7 1- CHEM :     387 TERMS
                SET SMARTSELECT OFF

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 14:52:36 ON 10 DEC 2010
L10        7444 S L8
L11        2046 S L9
L12        7703 S L6 OR L10 OR L7 OR L11
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L13        1330 S L12 AND (CANCER OR TUMOR OR TUMOUR OR NEOPLASM OR CARCINOMA)/
L14         397 S L13 AND PD<20010702
L15          12 S L14 AND (CYCLOPAMINE OR JERVINE)/AB
L16           5 DUP REM L15 (7 DUPLICATES REMOVED)

=> s hedgehog/ab and (cancer or tumor or tumour or neoplasm or carcinoma)/ab
L17       3679 HEDGEHOG/AB AND (CANCER OR TUMOR OR TUMOUR OR NEOPLASM OR CARCIN
               OMA)/AB

=> s l17 and pd<20010702
L18        313 L17 AND PD<20010702

=> dup rem l18
PROCESSING COMPLETED FOR L18
L19         138 DUP REM L18 (175 DUPLICATES REMOVED)

=> s l19 and (apoptosis or differentiation)
L20         27 L19 AND (APOPTOSIS OR DIFFERENTIATION)

=> d l20 1-27 ibib abs

L20  ANSWER 1 OF 27     MEDLINE on STN
ACCESSION NUMBER:   2002152875     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11886539
TITLE:              No evidence of deregulated patched-hedgehog signaling
                    pathway in trichoblastomas and other tumors arising within
                    nevus sebaceous.
AUTHOR:             Takata M; Tojo M; Hatta N; Ohara K; Yamada M; Takehara K
CORPORATE SOURCE:   Department of Dermatology, Kanazawa University School of
                    Medicine, Kanazawa, Japan.. takata@med.kanazawa-u.ac.jp
SOURCE:             The Journal of investigative dermatology, (2001
                    Dec) Vol. 117, No. 6, pp. 1666-70.
                    Journal code: 0426720. ISSN: 0022-202X. L-ISSN: 0022-202X.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200204
ENTRY DATE:         Entered STN: 12 Mar 2002
                    Last Updated on STN: 6 Apr 2002
                    Entered Medline: 5 Apr 2002
AB   Nevus sebaceous is a congenital malformation of the skin within which a
     number of neoplasms showing adnexal differentiation
     may arise.  Recently, deletions in the patched gene region were reported
     in nevus sebaceous and constitutive activation of the patched-
     hedgehog signaling pathway was implicated in the development of
     tumors arising within nevus sebaceous.  To substantiate further a
     role of the patched-hedgehog signaling pathway in secondary
     tumors arising within nevus sebaceous, we examined 11 nevus
     sebaceous associated with secondary tumors for loss of
     heterozygosity of the patched gene region by microsatellite polymerase
     chain reaction and patched mRNA expression by in situ hybridization.
     Unexpectedly, however, none of the tumors (including eight
     trichoblastomas) and nevus sebaceous lesions showed loss of heterozygosity
     at any polymorphic loci close to the patched gene.  Further more, none of
     the nevus sebaceous lesions and secondary tumors gave detectable
     signals for patched mRNA.  In contrast, four of 11 sporadic basal cell
     carcinomas, that were examined for comparison, showed loss of
     heterozygosity at the patched gene locus (p <0.05), and moderate to strong
     signals for patched mRNA was observed in all seven basal cell
     carcinoma tumors examined (p <0.0001).  Additional
     investigation by reverse transcription-polymerase chain reaction in four
     basal cell carcinomas and two nevus sebaceous tumors
     also showed the expression of Gli-1, another target gene in the patched-
     hedgehog signaling pathway, in all the basal cell
     carcinomas samples but not in any of the nevus sebaceous
     tumors examined.  The findings in this study do not support the
     view that the deregulation of the patched-hedgehog signaling
     pathway is involved in the pathogenesis of nevus sebaceous and associated
     tumors, and show that, although morphologically similar,
     trichoblastomas and basal cell carcinomas have a different
     molecular pathogenesis.

L20  ANSWER 2 OF 27     MEDLINE on STN
ACCESSION NUMBER:   2002036399     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11763995
TITLE:              Adenovirus-mediated increase of HNF-3 levels stimulates
                    expression of transthyretin and sonic hedgehog, which is
                    associated with F9 cell differentiation toward
                    the visceral endoderm lineage.
AUTHOR:             Tan Y; Costa R H; Kovesdi I; Reichel R R
CORPORATE SOURCE:   University of Illinois at Chicago, College of Medicine,
                    Department of Molecular Genetics, 60607-7170, USA..
                    ytan@uic.edu
CONTRACT NUMBER:    R01 GM43241-11 (United States NIGMS NIH HHS)
SOURCE:             Gene expression, (2001) Vol. 9, No. 6, pp.
                    237-48.
                    Journal code: 9200651. ISSN: 1052-2166. L-ISSN: 1052-2166.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
                    (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200205
ENTRY DATE:         Entered STN: 24 Jan 2002
                    Last Updated on STN: 3 May 2002
                    Entered Medline: 2 May 2002
AB   Retinoic acid-induced differentiation of mouse F9 embryonal
     carcinoma cells toward the visceral endoderm lineage is
     accompanied by increased expression of the Forkhead Box (Fox)
     transcription factors hepatocyte nuclear factor 3a (HNF-3alpha) and
     HNF-3beta, suggesting that they play a crucial role in visceral endoderm
     development.  Retinoic acid stimulation results in a cascade of HNF-3
     induction in which HNF-3alpha is a primary target for retinoic acid action
     and its increase is required for subsequent induction of HNF-3beta
     expression.  Increased expression of HNF-3beta precedes activation of its
     known target genes, including transthyretin (TTR), Sonic hedgehog
     (Shh), HNF-1alpha, HNF-1beta, and HNF-4alpha.  In order to examine whether
     increased HNF-3 expression is sufficient to induce expression of its
     downstream target genes without retinoic acid stimulation, we have used
     adenovirus-based expression vectors to increase HNF-3 protein levels in F9
     cells.  We demonstrate that adenovirus-mediated increase of HNF-3alpha
     levels in F9 cells is sufficient to induce activation of endogenous
     HNF-3beta levels followed by increased TTR and Shh expression.
     Furthermore, we show that elevated HNF-3beta levels stimulate expression
     of endogenous TTR and Shh without retinoic acid stimulation.  Moreover,
     ectopic HNF-3 levels in undifferentiated F9 cells are insufficient to
     induce HNF-3alpha, HNF-1alpha, HNF-1beta, and HNF-4alpha expression,
     suggesting that their transcriptional activation required other regulatory
     proteins induced by the retinoic acid differentiation program.
     Finally, our studies demonstrate the utility of cell infections with
     adenovirus expressing distinct transcription factors to identify
     endogenous target genes, which are assembled with the appropriate
     nucleosome structure.

L20  ANSWER 3 OF 27     MEDLINE on STN
ACCESSION NUMBER:   2002025304     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11485016
TITLE:              Role of receptor activator of nuclear factor-kappaB ligand
                    and osteoprotegerin in bone cell biology.
AUTHOR:             Hofbauer L C; Heufelder A E
CORPORATE SOURCE:   Division of Gastroenterology, Endocrinology and Metabolism,
                    Zentrum fur Innere Medizein, Philipps University, Marburg,
                    Germany.. hofbauer@post.med.uni-marburg.de
SOURCE:             Journal of molecular medicine (Berlin, Germany), (2001
                    Jun) Vol. 79, No. 5-6, pp. 243-53.  Ref: 138
                    Journal code: 9504370. ISSN: 0946-2716. L-ISSN: 0946-2716.
PUB. COUNTRY:       Germany: Germany, Federal Republic of
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200201
ENTRY DATE:         Entered STN: 21 Jan 2002
                    Last Updated on STN: 20 Apr 2002
                    Entered Medline: 25 Jan 2002
REFERENCE COUNT:    138  There are 138 cited references for this document.
AB   Receptor activator of nuclear factor (NF-kappaB) ligand (RANKL), its
     cellular receptor, receptor activator of NF-kappaB (RANK), and the decoy
     receptor osteoprotegerin (OPG) constitute a novel cytokine system.  RANKL
     produced by osteoblastic lineage cells and activated T lymphocytes is the
     essential factor for osteoclast formation, fusion, activation, and
     survival, thus resulting in bone resorption and bone loss.  RANKL
     activates its specific receptor, RANK located on osteoclasts and dendritic
     cells, and its signaling cascade involves stimulation of the c-jun,
     NF-kappaB, and serine/threonine kinase PKB/Akt pathways.  The effects of
     RANKL are counteracted by OPG which acts as a soluble neutralizing
     receptor.  RANKL and OPG are regulated by various hormones
     (glucocorticoids, vitamin D, estrogen), cytokines (tumor
     necrosis factor alpha, interleukins 1, 4, 6, 11, and 17), and various
     mesenchymal transcription factors (such as cbfa-1, peroxisome
     proliferator-activated receptor gamma, and Indian hedgehog).
     Transgenic and knock-out mice with excessive or defective production of
     RANKL, RANK, and OPG display the extremes of skeletal phenotypes,
     osteoporosis and osteopetrosis.  Abnormalities of the RANKL/OPG system
     have been implicated in the pathogenesis of postmenopausal osteoporosis,
     rheumatoid arthritis, Paget's disease, periodontal disease, benign and
     malignant bone tumors, bone metastases, and hypercalcemia of
     malignancy, while administration of OPG has been demonstrated to prevent
     or mitigate these disorders in animal models.  RANKL and OPG are also
     important regulators of vascular biology and calcification and of the
     development of a lactating mammary gland during pregnancy, indicating a
     crucial role for this system in extraskeletal calcium handling.  The
     discovery and characterization of RANKL, RANK, and OPG and subsequent
     studies have changed the concepts of bone and calcium metabolism, have led
     to a detailed understanding of the pathogenesis of metabolic bone
     diseases, and may form the basis of innovative therapeutic strategies.

L20  ANSWER 4 OF 27     MEDLINE on STN
ACCESSION NUMBER:   2001664465     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11711859
TITLE:              Expression of RA175 mRNA, a new member of the
                    immunoglobulin superfamily, in developing mouse brain.
AUTHOR:             Urase K; Soyama A; Fujita E; Momoi T
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CORPORATE SOURCE:    Division of Development and Differentiation, National
                     Institute of Neuroscience, NCNP, Kodaira, Tokyo 187-8502,
                     Japan.
SOURCE:              Neuroreport, (2001 Oct 29) Vol. 12, No. 15, pp.
                     3217-21.
                     Journal code: 9100935. ISSN: 0959-4965. L-ISSN: 0959-4965.
PUB. COUNTRY:        England: United Kingdom
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
                     (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
OTHER SOURCE:        GENBANK-AB021964; GENBANK-AB021965; GENBANK-AB021966
ENTRY MONTH:         200202
ENTRY DATE:          Entered STN: 19 Nov 2001
                     Last Updated on STN: 20 Feb 2002
                     Entered Medline: 19 Feb 2002
AB    RA175, a new member of the immunoglobulin superfamily, is highly expressed
      during neuronal differentiation of P19 embryonal
      carcinoma cells.  In situ hybridization showed that RA175 mRNA was
      detected in the developing nervous system, as well as the epithelium of
      the various non-neuronal tissues of mouse embryo.  In contrast with the
      epithelia of the non-neuronal tissues, RA175 mRNA was not co-expressed
      with Sonic hedgehog mRNA and Patched mRNA during brain
      morphogenesis.  RA175 mRNA was highly expressed in the anterior horn cells
      and the peripheral nervous system at embryonic day (E) 11.5 and in the
      central nervous system at E14.5-E18.5, but its expression decreased after
      birth and was undetectable in the adult mouse brain.

L20  ANSWER 5 OF 27     MEDLINE on STN
ACCESSION NUMBER:    2001610514     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 11684448
TITLE:               UV-induced DNA damage, repair, mutations and oncogenic
                     pathways in skin cancer.
AUTHOR:              de Gruijl F R; van Kranen H J; Mullenders L H
CORPORATE SOURCE:    Department of Dermatology, Sylvius Lab, Leiden Univ. Med.
                     Ctr., Wassenaarseweg 72, NL-2333 AL Leiden, The
                     Netherlands.. f.r.de_gruijl@lumc.nl
SOURCE:              Journal of photochemistry and photobiology. B, Biology,
                     (2001 Oct) Vol. 63, No. 1-3, pp. 19-27.  Ref: 82
                     Journal code: 8804966. ISSN: 1011-1344. L-ISSN: 1011-1344.
PUB. COUNTRY:        Switzerland
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
                     (RESEARCH SUPPORT, NON-U.S. GOV'T)
                     General Review; (REVIEW)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200201
ENTRY DATE:          Entered STN: 2 Nov 2001
                     Last Updated on STN: 25 Jan 2002
                     Entered Medline: 22 Jan 2002
REFERENCE COUNT:     82   There are 82 cited references for this document.
AB    Repair of UV induced DNA damage is of key importance to UV-induced skin
      carcinogenesis.  Specific signal transduction pathways that regulate cell
      cycling, differentiation and apoptosis are found to be
      corrupted in skin cancers, e.g., the epidermal
      growth-stimulating Hedgehog pathway in basal cell
      carcinomas (BCCs).  Mutations in genes coding for proteins in
      these pathways lead to persistent disturbances that are passed along to
      daughter cells, e.g., mutations in the gene for the Patched (PTCH) protein
      in the Hedgehog pathway.  Thus far only the point mutations in
      the P53 gene from squamous cell carcinomas and BCCs, and in PTCH
      gene from BCC of xeroderma pigmentosum (XP) patients appear to be
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     unambiguously attributable to solar UV radiation.  Solar UVB radiation is
     most effective in causing these point mutations.  Other forms of
     UV-induced genetic changes (e.g., deletions) may, however, contribute to
     skin carcinogenesis with different wavelength dependencies.

L20  ANSWER 6 OF 27     MEDLINE on STN
ACCESSION NUMBER:   2001504570     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11283316
TITLE:              The developmental biology of brain tumors.
AUTHOR:             Wechsler-Reya R; Scott M P
CORPORATE SOURCE:   Department of Developmental Biology and Howard Hughes
                    Medical Institute, Stanford University School of Medicine,
                    Stanford, California 94305-5329, USA..
                    rwreya@cmgm.stanford.edu
SOURCE:             Annual review of neuroscience, (2001) Vol. 24,
                    pp. 385-428.  Ref: 325
                    Journal code: 7804039. ISSN: 0147-006X. L-ISSN: 0147-006X.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200109
ENTRY DATE:         Entered STN: 17 Sep 2001
                    Last Updated on STN: 17 Sep 2001
                    Entered Medline: 13 Sep 2001
REFERENCE COUNT:    325  There are 325 cited references for this document.
AB   Tumors of the central nervous system (CNS) can be devastating
     because they often affect children, are difficult to treat, and frequently
     cause mental impairment or death.  New insights into the causes and
     potential treatment of CNS tumors have come from discovering
     connections with genes that control cell growth, differentiation
     , and death during normal development.  Links between tumorigenesis and
     normal development are illustrated by three common CNS tumors:
     retinoblastoma, glioblastoma, and medulloblastoma.  For example, the
     retinoblastoma (Rb) tumor suppressor protein is crucial for
     control of normal neuronal differentiation and apoptosis
     .  Excessive activity of the epidermal growth factor receptor and loss of
     the phosphatase PTEN are associated with glioblastoma, and both genes are
     required for normal growth and development.  The membrane protein Patched1
     (Ptc1), which controls cell fate in many tissues, regulates cell growth in
     the cerebellum, and reduced Ptc1 function contributes to medulloblastoma.
     Just as elucidating the mechanisms that control normal development can
     lead to the identification of new cancer-related genes and
     signaling pathways, studies of tumor biology can increase our
     understanding of normal development.  Learning that Ptc1 is a
     medulloblastoma tumor suppressor led directly to the
     identification of the Ptc1 ligand, Sonic hedgehog, as a powerful
     mitogen for cerebellar granule cell precursors.  Much remains to be
     learned about the genetic events that lead to brain tumors and
     how each event regulates cell cycle progression, apoptosis, and
     differentiation.  The prospects for beneficial work at the
     boundary between oncology and developmental biology are great.

L20  ANSWER 7 OF 27     MEDLINE on STN
ACCESSION NUMBER:   2001490052     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11532396
TITLE:              Monstrous attempts at adnexogenesis: regulating hair
                    follicle progenitors through Sonic hedgehog signaling.
AUTHOR:             Callahan C A; Oro A E
CORPORATE SOURCE:   Program in Epithelial Biology, Stanford University, CCSR
                    Building, Room 2145, 269 Campus Drive, Stanford, CA
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                        94305-5168, USA.
CONTRACT NUMBER:        AR46786 (United States NIAMS NIH HHS)
SOURCE:                 Current opinion in genetics & development, (2001
                        Oct) Vol. 11, No. 5, pp. 541-6.  Ref: 48
                        Journal code: 9111375. ISSN: 0959-437X. L-ISSN: 0959-437X.
PUB. COUNTRY:           England: United Kingdom
DOCUMENT TYPE:          Journal; Article; (JOURNAL ARTICLE)
                        (RESEARCH SUPPORT, NON-U.S. GOV'T)
                        (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
                        General Review; (REVIEW)
LANGUAGE:               English
FILE SEGMENT:           Priority Journals
ENTRY MONTH:            200112
ENTRY DATE:             Entered STN: 5 Sep 2001
                        Last Updated on STN: 22 Jan 2002
                        Entered Medline: 4 Dec 2001
REFERENCE COUNT:        48   There are 48 cited references for this document.
AB   Epithelial organs such as the vertebrate hair control periodic
     self-renewal by regulating the growth of progenitor cells.  Recent studies
     implicate Sonic hedgehog target gene induction in the growth of
     multipotent hair follicle epithelium and the development of a variety of
     hair follicle tumors such as basal cell carcinomas.
     These studies suggest Sonic hedgehog signaling may regulate
     progenitor cells in other organs.

L20  ANSWER 8 OF 27     MEDLINE on STN
ACCESSION NUMBER:       2001479307     MEDLINE
DOCUMENT NUMBER:        PubMed ID: 11523056
TITLE:                  Expression of the Sonic Hedgehog receptor "PATCHED" in
                        basal cell carcinomas and odontogenic keratocysts.
AUTHOR:                 Zedan W; Robinson P A; Markham A F; High A S
CORPORATE SOURCE:       Molecular Medicine Unit, University of Leeds, Clinical
                        Sciences Building, St James's University Hospital, Leeds,
                        LS9 7TF, UK.
SOURCE:                 The Journal of pathology, (2001 Aug) Vol. 194,
                        No. 4, pp. 473-7.
                        Journal code: 0204634. ISSN: 0022-3417. L-ISSN: 0022-3417.
PUB. COUNTRY:           England: United Kingdom
DOCUMENT TYPE:          Journal; Article; (JOURNAL ARTICLE)
                        (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:               English
FILE SEGMENT:           Priority Journals
ENTRY MONTH:            200109
ENTRY DATE:             Entered STN: 28 Aug 2001
                        Last Updated on STN: 1 Oct 2001
                        Entered Medline: 27 Sep 2001
AB   Basal cell carcinoma (BCC) is a common invasive skin lesion in
     Caucasians.  Odontogenic keratocysts (OKs) are developmental,
     non-inflammatory oral cysts.  They can be sporadic and/or multiple and are
     locally destructive.  Basal cell naevus syndrome (BCNS) comprises both
     multiple BCCs and multiple OKs, in addition to several other systemic
     manifestations.  The genetic defect underlying this autosomal dominant
     syndrome is a germ line mutation in the Sonic Hedgehog receptor
     PATCHED (PTCH) gene.  For this study, a rabbit anti-peptide PTCH antiserum
     was produced.  Immunohistochemistry procedures were performed using PTCH
     antibody and commercially produced GLI-1 antibody (downstream member in
     the hedgehog pathway) to stain 11 BCNS-OKs, eight sporadic OKs,
     two BCNS-BCCs, and six sporadic BCCs.  Most of these lesions had been
     previously screened for PTCH mutation.  Most BCCs (n=7) demonstrated
     moderate staining, with the heaviest staining in the outer palisading cell
     layer, except a BCNS-BCC which had mutation proximal to the sequence used
     for production of immunogenic peptide; this demonstrated only weak
     staining.  Although moderate to heavy staining with PTCH antibody was
     demonstrated in the epithelium of both types of OK (n=19), a quite
     different pattern of staining of the basal cell layer was observed in the
     two patient groups.  In BCNS, OK staining was heaviest in basal epithelial
     layers.  In contrast, staining in non-BCNS odontogenic keratocysts was
     exclusively located in the superficial epithelial layers.  Up-regulation
     of PTCH and GLI-1 protein was demonstrated in both BCCs and OKs.  The
     pattern of PTCH expression matched the PTCH transcript pattern previously
     reported in BCCs and appeared sufficiently characteristic in OKs to allow
     differentiation between syndromic and non-syndromic cysts.
     Copyright 2001 John Wiley & Sons, Ltd.

L20  ANSWER 9 OF 27     MEDLINE on STN
ACCESSION NUMBER:   2001400763     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11452312
TITLE:              Insights into Wnt binding and signalling from the
                    structures of two Frizzled cysteine-rich domains.
AUTHOR:             Dann C E; Hsieh J C; Rattner A; Sharma D; Nathans J; Leahy
                    D J
CORPORATE SOURCE:   Department of Biophysics and Biophysical Chemistry, Johns
                    Hopkins University School of Medicine, Baltimore, MD 21205,
                    USA.
SOURCE:             Nature, (2001 Jul 5) Vol. 412, No. 6842, pp.
                    86-90.
                    Journal code: 0410462. ISSN: 0028-0836. L-ISSN: 0028-0836.
PUB. COUNTRY:       England: United Kingdom
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
OTHER SOURCE:       PDB-1IJX; PDB-1IJY
ENTRY MONTH:        200107
ENTRY DATE:         Entered STN: 30 Jul 2001
                    Last Updated on STN: 30 Jul 2001
                    Entered Medline: 26 Jul 2001
AB   Members of the Frizzled family of seven-pass transmembrane proteins serve
     as receptors for Wnt signalling proteins.  Wnt proteins have important
     roles in the differentiation and patterning of diverse tissues
     during animal development, and inappropriate activation of Wnt signalling
     pathways is a key feature of many cancers.  An extracellular
     cysteine-rich domain (CRD) at the amino terminus of Frizzled proteins
     binds Wnt proteins, as do homologous domains in soluble proteins-termed
     secreted Frizzled-related proteins-that function as antagonists of Wnt
     signalling.  Recently, an LDL-receptor-related protein has been shown to
     function as a co-receptor for Wnt proteins and to bind to a Frizzled CRD
     in a Wnt-dependent manner.  To investigate the molecular nature of the Wnt
     signalling complex, we determined the crystal structures of the CRDs from
     mouse Frizzled 8 and secreted Frizzled-related protein 3.  Here we show a
     previously unknown protein fold, and the design and interpretation of CRD
     mutations that identify a Wnt-binding site.  CRDs exhibit a conserved
     dimer interface that may be a feature of Wnt signalling.  This work
     provides a framework for studies of homologous CRDs in proteins including
     muscle-specific kinase and Smoothened, a component of the Hedgehog
     signalling pathway.

L20  ANSWER 10 OF 27     MEDLINE on STN
ACCESSION NUMBER:   2001355663     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11257109
TITLE:              The hedgehog pathway and basal cell carcinomas.
AUTHOR:             Bale A E; Yu K P
CORPORATE SOURCE:   Department of Genetics, SHM I-321, Yale University School
                    of Medicine, Box 208005, 333 Cedar Street, New Haven, CT
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                        06520-8005, USA.. allen.bale@yale.edu
SOURCE:                 Human molecular genetics, (2001 Apr) Vol. 10, No.
                        7, pp. 757-62.  Ref: 73
                        Journal code: 9208958. ISSN: 0964-6906. L-ISSN: 0964-6906.
PUB. COUNTRY:           England: United Kingdom
DOCUMENT TYPE:          Journal; Article; (JOURNAL ARTICLE)
                        General Review; (REVIEW)
LANGUAGE:               English
FILE SEGMENT:           Priority Journals
ENTRY MONTH:            200106
ENTRY DATE:             Entered STN: 25 Jun 2001
                        Last Updated on STN: 25 Jun 2001
                        Entered Medline: 21 Jun 2001
REFERENCE COUNT:        73   There are 73 cited references for this document.
AB   Developmental pathways first elucidated by genetic studies in the fruit
     fly, Drosophila melanogaster, are conserved in vertebrates, and disruption
     of these pathways has been associated with various human congenital
     anomalies.  Many developmental genes continue to play an important role in
     regulation of cell growth and differentiation after
     embryogenesis, and mutations in some of these genes can result in
     cancer.  Basal cell carcinoma (BCC) of the skin is the
     most common type of cancer in humans.  Although most BCCs are
     sporadic, in rare cases, individuals have a hereditary disease, Gorlin
     syndrome, that predisposes to multiple skin tumors as well as a
     variety of birth defects.  Mutations in the human homolog of a Drosophila
     gene, patched, underlie Gorlin syndrome.  Genetic studies in Drosophila
     show that patched is part of the hedgehog signaling pathway,
     important in determining embryonic patterning and cell fate in multiple
     structures of the developing embryo.  Human patched is mutated in sporadic
     as well as hereditary BCCs, and inactivation of this gene is probably a
     necessary if not sufficient step for tumor formation.
     Delineation of the biochemical pathway in which patched functions may lead
     to rational medical therapy for skin cancer and possibly other
     tumors.

L20  ANSWER 11 OF 27     MEDLINE on STN
ACCESSION NUMBER:       2001112888     MEDLINE
DOCUMENT NUMBER:        PubMed ID: 11133163
TITLE:                  Downregulation of Hedgehog signaling is required for
                        organogenesis of the small intestine in Xenopus.
AUTHOR:                 Zhang J; Rosenthal A; de Sauvage F J; Shivdasani R A
CORPORATE SOURCE:       Department of Molecular Oncology, Genentech, Inc., South
                        San Francisco, California 94080, USA.
SOURCE:                 Developmental biology, (2001 Jan 1) Vol. 229, No.
                        1, pp. 188-202.
                        Journal code: 0372762. ISSN: 0012-1606. L-ISSN: 0012-1606.
PUB. COUNTRY:           United States
DOCUMENT TYPE:          (COMPARATIVE STUDY)
                        Journal; Article; (JOURNAL ARTICLE)
                        (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:               English
FILE SEGMENT:           Priority Journals
ENTRY MONTH:            200102
ENTRY DATE:             Entered STN: 22 Mar 2001
                        Last Updated on STN: 22 Mar 2001
                        Entered Medline: 8 Feb 2001
AB   Hedgehog ligands interact with receptor complexes containing
     Patched (PTC) and Smoothened (SMO) proteins to regulate many aspects of
     development.  The mutation W535L (SmoM2) in human Smo is associated with
     basal cell skin cancers, causes constitutive, ligand-independent
     signaling through the Hedgehog pathway, and provides a powerful
     means to test effects of unregulated Hedgehog signaling.
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Expression of SmoM2 in Xenopus embryos leads to developmental anomalies that are consistent with known requirements for regulated Hedgehog signaling in the eye and pancreas. Additionally, it results in failure of midgut epithelial cytodifferentiation and of the intestine to lengthen and coil. The midgut mesenchyme shows increased cell numbers and attenuated expression of the differentiation marker smooth muscle actin. With the exception of the pancreas, differentiation of foregut and hindgut derivatives is unaffected. The intestinal epithelial abnormalities are reproduced in embryos or organ explants treated directly with active recombinant hedgehog protein. Ptc mRNA, a principal target of Hedgehog signaling, is maximally expressed at stages corresponding to the onset of the intestinal defects. In advanced embryos expressing SmoM2, Ptc expression is remarkably confined to the intestinal wall. Considered together, these findings suggest that the splanchnic mesoderm responds to endodermal Hedgehog signals by inhibiting the transition of midgut endoderm into intestinal epithelium and that attenuation of this feedback is required for normal development of the vertebrate intestine.
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L20 ANSWER 12 OF 27 MEDLINE on STN
ACCESSION NUMBER: 2001087248 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11140704
TITLE: Up-regulation of PTHrP and Bcl-2 expression characterizes the progression of osteochondroma towards peripheral chondrosarcoma and is a late event in central chondrosarcoma.
AUTHOR: Bovee J V; van den Broek L J; Cleton-Jansen A M; Hogendoorn P C
CORPORATE SOURCE: Department of Pathology, Leiden University Medical Center, The Netherlands.. J.V.M.G.Bovee@lumc.nl
SOURCE: Laboratory investigation; a journal of technical methods and pathology, (2000 Dec) Vol. 80, No. 12, pp. 1925-34.
Journal code: 0376617. ISSN: 0023-6837. L-ISSN: 0023-6837.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 11 Jan 2003
Entered Medline: 18 Jan 2001

AB Chondrosarcomas are malignant cartilage-forming tumors arising centrally in bone (central chondrosarcoma) or within the cartilaginous cap of osteochondroma (peripheral chondrosarcoma). For hereditary multiple osteochondromas, two responsible genes, EXT1 and EXT2, have been cloned. Their recently elucidated role in heparan sulfate biosynthesis and Hedgehog diffusion leads to the hypothesis that EXT inactivation affects fibroblast growth factor (FGF) and Indian Hedgehog (IHh)/parathyroid hormone-related peptide (PTHrP) signaling, two important pathways in chondrocyte proliferation and differentiation. The expression of PTHrP, PTHrP-receptor, Bcl-2, FGF2, FGFR1, FGFR3, and p21 is investigated by immunohistochemistry in osteochondromas (n = 24) and peripheral (n = 29) and central (n = 20) chondrosarcomas. IHh/PTHrP and FGF signaling molecules are mostly absent in osteochondromas. Although no somatic EXT mutations were found in sporadic osteochondromas, the putative EXT downstream targets are affected similarly in sporadic and hereditary tumors. In chondrosarcomas, re-expression of FGF2, FGFR1, PTHrP, Bcl-2, and p21 is found. Expression levels increase with increasing histological grade. Up-regulation of PTHrP and Bcl-2 characterizes malignant transformation of osteochondroma because PTHrP and Bcl-2

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     expression is significantly higher in borderline and grade I peripheral
     chondrosarcomas compared with osteochondromas.  In contrast, up-regulation
     of PTHrP and Bcl-2 seems to be a late event in central cartilaginous
     tumorigenesis because expression is mainly restricted to high-grade
     central tumors.

L20  ANSWER 13 OF 27     MEDLINE on STN
ACCESSION NUMBER:   2000485416     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11034076
TITLE:              Regulation of gli activity by all-trans retinoic acid in
                    mouse keratinocytes.
AUTHOR:             Goyette P; Allan D; Peschard P; Chen C F; Wang W; Lohnes D
CORPORATE SOURCE:   Department of Molecular Biology, Universite de Montreal,
                    Quebec, Canada.
SOURCE:             Cancer research, (2000 Oct 1) Vol. 60, No. 19,
                    pp. 5386-9.
                    Journal code: 2984705R. ISSN: 0008-5472. L-ISSN: 0008-5472.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200010
ENTRY DATE:         Entered STN: 22 Mar 2001
                    Last Updated on STN: 22 Mar 2001
                    Entered Medline: 27 Oct 2000
AB   Sonic hedgehog (Shh) signaling is essential for many normal
     developmental processes.  The Shh signal is interpreted by the Gli
     transcription factors.  Elevated Gli-1 expression has been associated with
     several neoplasms, including basal cell carcinoma.
     All-trans retinoic acid (RA) has strong effects on epidermal growth and
     differentiation and has been used for the treatment of various
     epithelial disorders.  In this report, we show that RA can inhibit Gli
     activity in immortalized murine keratinocytes in a RA receptor-specific
     manner.  This inhibition may occur, at least in part, through
     sequestration of the transcriptional coactivator cyclic AMP-responsive
     element-binding protein-binding protein and suggests a novel effect of
     retinoid excess on Shh signaling.

L20  ANSWER 14 OF 27     MEDLINE on STN
ACCESSION NUMBER:   2000191326     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 10728982
TITLE:              The impact of developmental biology on cancer research: an
                    overview.
AUTHOR:             Edwards P A
CORPORATE SOURCE:   Department of Pathology, University of Cambridge, UK..
                    pawe1@cam.ac.uk
SOURCE:             Cancer metastasis reviews, (1999) Vol. 18, No. 2,
                    pp. 175-80.  Ref: 19
                    Journal code: 8605731. ISSN: 0167-7659. L-ISSN: 0167-7659.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200004
ENTRY DATE:         Entered STN: 21 Apr 2000
                    Last Updated on STN: 21 Apr 2000
                    Entered Medline: 13 Apr 2000
REFERENCE COUNT:    19   There are 19 cited references for this document.
AB   In recent years developmental biology has contributed a great deal to
     cancer research.  This is in part because both fields address the
     question of how genes control the three-dimensional organisation of
     tissues, and how mutation of genes alters this.  But also in recent years,
     the discovery that signalling pathways are conserved from worms to man,
     combined with the power of developmental biology's model organisms,
     principally Drosophila and C. elegans, to reveal signalling pathways that
     control tissue growth and organisation, has had a huge impact.  Examples
     of this are the subject of the reviews in this issue, including the
     EGF-receptor, Wnt/APC/catenin, TGF-beta/Smad and hedgehog
     /patched/smoothened pathways, all of which were discovered and/or pieced
     together in model organisms, and all of which are disrupted by mutation in
     human cancer.  Other topics considered are the control and
     execution of apoptosis; the search for tumour
     -suppressor-like genes in Drosophila; and genes of the Polycomb and
     Trithorax Groups that regulate the commitment of cells to patterns of
     differentiation, and that are among the targets for chromosome
     translocations.  These stories illustrate how developmental biology has
     shown that there are many more signalling pathways relevant to neoplasia
     than the receptor tyrosine kinase pathways that first dominated the field;
     and that the signalling is more than just mitogenic or anti-mitogenic, and
     should be viewed as providing cells with information about their position
     and neighbours, that determines their role, differentiation and
     behaviour.

L20  ANSWER 15 OF 27     MEDLINE on STN
ACCESSION NUMBER:   2000047795     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 10579908
TITLE:              Hedgehog signal transduction: from flies to vertebrates.
AUTHOR:             Murone M; Rosenthal A; de Sauvage F J
CORPORATE SOURCE:   Department of Molecular Oncology, Department of
                    Neuroscience, Genentech, Inc., One DNA Way, South San
                    Francisco, California, 94080, USA.
SOURCE:             Experimental cell research, (1999 Nov 25) Vol.
                    253, No. 1, pp. 25-33.  Ref: 104
                    Journal code: 0373226. ISSN: 0014-4827. L-ISSN: 0014-4827.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199912
ENTRY DATE:         Entered STN: 14 Jan 2000
                    Last Updated on STN: 10 Dec 2002
                    Entered Medline: 30 Dec 1999
REFERENCE COUNT:    104  There are 104 cited references for this document.
AB   The patterning and morphogenesis of multicellular organisms require a
     complex interplay of inductive signals which control proliferation, growth
     arrest, and differentiation of different cell types.  A number
     of such signaling molecules have been identified in vertebrates and
     invertebrates.  The molecular dissection of these pathways demonstrated
     that in vertebrates, mutations or abnormals function of these signaling
     pathways were often associated with developmental disorders and
     cancer formation.  The Hedgehog (Hh) family of secreted
     proteins provides a perfect example of such signaling proteins.  In the
     following review, we will not discuss in detail the role of Hh as a
     morphogen, but rather focus on its signal transduction pathway and its
     role in various human disorders.
     Copyright 1999 Academic Press.

L20  ANSWER 16 OF 27     MEDLINE on STN
ACCESSION NUMBER:   1999448190     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 10516314
TITLE:              Sonic hedgehog regulates proliferation and inhibits
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                        differentiation of CNS precursor cells.
AUTHOR:                 Rowitch D H; S-Jacques B; Lee S M; Flax J D; Snyder E Y;
                        McMahon A P
CORPORATE SOURCE:       Department of Molecular and Cellular Biology, Harvard
                        University, Cambridge, Massachusetts 02138, USA.
CONTRACT NUMBER:        HD01182 (United States NICHD NIH HHS)
                        HD30249 (United States NICHD NIH HHS)
                        NS32691 (United States NINDS NIH HHS)
SOURCE:                 The Journal of neuroscience : the official journal of the
                        Society for Neuroscience, (1999 Oct 15) Vol. 19,
                        No. 20, pp. 8954-65.
                        Journal code: 8102140. E-ISSN: 1529-2401. L-ISSN:
                        0270-6474.
PUB. COUNTRY:           United States
DOCUMENT TYPE:          Journal; Article; (JOURNAL ARTICLE)
                        (RESEARCH SUPPORT, NON-U.S. GOV'T)
                        (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE:               English
FILE SEGMENT:           Priority Journals
ENTRY MONTH:            199910
ENTRY DATE:             Entered STN: 11 Jan 2000
                        Last Updated on STN: 21 May 2001
                        Entered Medline: 28 Oct 1999
AB   Activation of the Sonic hedgehog (Shh) signal transduction
     pathway is essential for normal pattern formation and cellular
     differentiation in the developing CNS.  However, it is also
     thought to be etiological in primitive neuroectodermal tumors.
     We adapted GAL4/UAS methodology to ectopically express full-length Shh in
     the dorsal neural tube of transgenic mouse embryos commencing at 10 d
     postcoitum (dpc), beyond the period of primary dorsal-ventral pattern
     formation and floorplate induction.  Expression of Shh was maintained
     until birth, permitting us to investigate effects of ongoing exposure to
     Shh on CNS precursors in vivo.  Proliferative rates of spinal cord
     precursors were twice that of wild-type littermates at 12.5 dpc.  In
     contrast, at late fetal stages (18.5 dpc), cells that were Shh-responsive
     but postmitotic were present in persistent structures reminiscent of the
     ventricular zone germinal matrix.  This tissue remained blocked in an
     undifferentiated state.  These results indicate that cellular competence
     restricts the proliferative response to Shh in vivo and provide evidence
     that proliferation and differentiation can be regulated
     separately in precursor cells of the spinal cord.  Thus, Hedgehog
     signaling may contribute to CNS tumorigenesis by directly enhancing
     proliferation and preventing neural differentiation in selected
     precursor cells.

L20  ANSWER 17 OF 27     MEDLINE on STN
ACCESSION NUMBER:       1999439758     MEDLINE
DOCUMENT NUMBER:        PubMed ID: 10508856
TITLE:                  Sonic hedgehog opposes epithelial cell cycle arrest.
AUTHOR:                 Fan H; Khavari P A
CORPORATE SOURCE:       VA Palo Alto Health Care System, Palo Alto, California
                        94304, USA.
CONTRACT NUMBER:        AR43799 (United States NIAMS NIH HHS)
                        AR44012 (United States NIAMS NIH HHS)
                        AR45192 (United States NIAMS NIH HHS)
SOURCE:                 The Journal of cell biology, (1999 Oct 4) Vol.
                        147, No. 1, pp. 71-6.
                        Journal code: 0375356. ISSN: 0021-9525. L-ISSN: 0021-9525.
                        Report No.: NLM-PMC2164980.
PUB. COUNTRY:           United States
DOCUMENT TYPE:          Journal; Article; (JOURNAL ARTICLE)
                        (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
                        (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE:               English
FILE SEGMENT:           Priority Journals
ENTRY MONTH:            199911
ENTRY DATE:             Entered STN: 11 Jan 2000
                        Last Updated on STN: 11 Jan 2000
                        Entered Medline: 4 Nov 1999
MEDLINE REFERENCE COUNT:   30    There are 30 cited references available in
                                 MEDLINE for this document.
AB   Stratified epithelium displays an equilibrium between proliferation and
     cell cycle arrest, a balance that is disrupted in basal cell
     carcinoma (BCC).  Sonic hedgehog (Shh) pathway
     activation appears sufficient to induce BCC, however, the way it does so
     is unknown.  Shh-induced epidermal hyperplasia is accompanied by continued
     cell proliferation in normally growth arrested suprabasal cells in vivo.
     Shh-expressing cells fail to exit S and G2/M phases in response to
     calcium-induced differentiation and also resist exhaustion of
     replicative growth capacity.  In addition, Shh blocks
     p21(CIP1/WAF1)-induced growth arrest.  These data indicate that Shh
     promotes neoplasia by opposing normal stimuli for epithelial cell cycle
     arrest.

L20  ANSWER 18 OF 27     MEDLINE on STN
ACCESSION NUMBER:   1999307074     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 10375501
TITLE:              Sonic hedgehog regulates the growth and patterning of the
                    cerebellum.
AUTHOR:             Dahmane N; Ruiz i Altaba A
CORPORATE SOURCE:   The Skirball Institute, Developmental Genetics Program and
                    Department of Cell Biology, NYU School of Medicine, New
                    York, NY 10016, USA.. ria@saturn.med.nyu.edu
CONTRACT NUMBER:    CA78736 (United States NCI NIH HHS)
SOURCE:             Development (Cambridge, England), (1999 Jun) Vol.
                    126, No. 14, pp. 3089-100.
                    Journal code: 8701744. ISSN: 0950-1991. L-ISSN: 0950-1991.
PUB. COUNTRY:       ENGLAND: United Kingdom
DOCUMENT TYPE:      (IN VITRO)
                    Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
                    (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199908
ENTRY DATE:         Entered STN: 27 Aug 1999
                    Last Updated on STN: 27 Aug 1999
                    Entered Medline: 19 Aug 1999
AB   The molecular bases of brain development and CNS malignancies remain
     poorly understood.  Here we show that Sonic hedgehog (Shh)
     signaling controls the development of the cerebellum at multiple levels.
     SHH is produced by Purkinje neurons, it is required for the proliferation
     of granule neuron precursors and it induces the differentiation
     of Bergmann glia.  Blocking SHH function in vivo results in deficient
     granule neuron and Bergmann glia differentiation as well as in
     abnormal Purkinje neuron development.  Thus, our findings provide a
     molecular model for the growth and patterning of the cerebellum by SHH
     through the coordination of the development of cortical cerebellar cell
     types.  In addition, they provide a cellular context for medulloblastomas,
     childhood cancers of the cerebellum.

L20  ANSWER 19 OF 27     MEDLINE on STN
ACCESSION NUMBER:   1999307008     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 10377278
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TITLE:               Pancreas development and diabetes.
AUTHOR:              St-Onge L; Wehr R; Gruss P
CORPORATE SOURCE:    DeveloGen AG Rudolf-Wissell-Strasse 28 D-37079, Gottingen,
                     Germany.. St-Onge@develogen.com
SOURCE:              Current opinion in genetics & development, (1999
                     Jun) Vol. 9, No. 3, pp. 295-300.  Ref: 44
                     Journal code: 9111375. ISSN: 0959-437X. L-ISSN: 0959-437X.
PUB. COUNTRY:        ENGLAND: United Kingdom
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
                     General Review; (REVIEW)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200003
ENTRY DATE:          Entered STN: 27 Mar 2000
                     Last Updated on STN: 27 Mar 2000
                     Entered Medline: 16 Mar 2000
REFERENCE COUNT:     44   There are 44 cited references for this document.
AB    The past few years have seen an increase in interest about the molecular
      and genetic events regulating pancreas development.  Transcription factors
      such as Pdx1, p48 and Nkx2.2 have been shown to be essential for the
      proper differentiation of exocrine and endocrine tissue;
      however, pancreas development also involves intricate interactions between
      the pancreatic epithelium and its surrounding mesenchyme.  Signalling
      factors emanating from the notochord have been shown to repress Sonic
      hedgehog expression in the endoderm whereas signals originating
      from the pancreatic mesenchyme determine the proportion of exocrine to
      endocrine tissue.  Understanding the molecular and genetic events
      underlying pancreas development also opens the door for devising new
      therapeutic strategies against pancreatic diseases such as diabetes and
      cancer.

L20  ANSWER 20 OF 27     MEDLINE on STN
ACCESSION NUMBER:    1999102111     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 9882493
TITLE:               Essential role for Sonic hedgehog during hair follicle
                     morphogenesis.
AUTHOR:              Chiang C; Swan R Z; Grachtchouk M; Bolinger M; Litingtung
                     Y; Robertson E K; Cooper M K; Gaffield W; Westphal H;
                     Beachy P A; Dlugosz A A
CORPORATE SOURCE:    Laboratory of Mammalian Genes and Development, National
                     Institutes of Health, Bethesda, Maryland, 20892, USA.
SOURCE:              Developmental biology, (1999 Jan 1) Vol. 205, No.
                     1, pp. 1-9.
                     Journal code: 0372762. ISSN: 0012-1606. L-ISSN: 0012-1606.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199902
ENTRY DATE:          Entered STN: 23 Feb 1999
                     Last Updated on STN: 23 Feb 1999
                     Entered Medline: 5 Feb 1999
AB    The hair follicle is a source of epithelial stem cells and site of origin
      for several types of skin tumors.  Although it is clear that
      follicles arise by way of a series of inductive tissue interactions,
      identification of the signaling molecules driving this process remains a
      major challenge in skin biology.  In this study we report an obligatory
      role for the secreted morphogen Sonic hedgehog (Shh) during hair
      follicle development.  Hair germs comprising epidermal placodes and
      associated dermal condensates were detected in both control and Shh -/-
      embryos, but progression through subsequent stages of follicle development
      was blocked in mutant skin.  The expression of Gli1 and Ptc1 was reduced
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     in Shh -/- dermal condensates and they failed to evolve into hair follicle
     papillae, suggesting that the adjacent mesenchyme is a critical target for
     placode-derived Shh.  Despite the profound inhibition of hair follicle
     morphogenesis, late-stage follicle differentiation markers were
     detected in Shh -/- skin grafts, as well as cultured vibrissa explants
     treated with cyclopamine to block Shh signaling.  Our findings reveal an
     essential role for Shh during hair follicle morphogenesis, where it is
     required for normal advancement beyond the hair germ stage of development.
     Copyright 1999 Academic Press.

L20  ANSWER 21 OF 27     MEDLINE on STN
ACCESSION NUMBER:   1998315043     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 9649421
TITLE:              Transducing Hedgehog: the story so far.
AUTHOR:             Ingham P W
CORPORATE SOURCE:   Developmental Genetics Programme, The Krebs Institute,
                    University of Sheffield, Sheffield S10 2TN, UK.
SOURCE:             The EMBO journal, (1998 Jul 1) Vol. 17, No. 13,
                    pp. 3505-11.  Ref: 80
                    Journal code: 8208664. ISSN: 0261-4189. L-ISSN: 0261-4189.
                    Report No.: NLM-PMC1170687.
PUB. COUNTRY:       ENGLAND: United Kingdom
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199808
ENTRY DATE:         Entered STN: 3 Sep 1998
                    Last Updated on STN: 10 Dec 2002
                    Entered Medline: 21 Aug 1998
REFERENCE COUNT:    80   There are 80 cited references for this document.
MEDLINE REFERENCE COUNT:   80    There are 80 cited references available in
                                 MEDLINE for this document.
AB   The secreted proteins of the Hedgehog family have been
     implicated in many different processes in vertebrate development including
     cartilage differentiation, myotome and sclerotome specification,
     hair follicle development, limb morphogenesis and the specification of
     different neuronal cell types.  In addition, the aberrant activation of
     the Hedgehog pathway has been identified as the likely cause of
     a number of tumours in humans including basal cell
     carcinomas (BCCs) and primitive neurectodermal tumours
     (PNETs).  Elucidating the mechanisms by which Hedgehog signals
     are transduced will thus have widespread implications for our
     understanding of both normal development and disease.

L20  ANSWER 22 OF 27     MEDLINE on STN
ACCESSION NUMBER:   1998286963     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 9625299
TITLE:              Hedgehog's escape from Pandora's box.
AUTHOR:             Currie P D
CORPORATE SOURCE:   Molecular Embryology Laboratory, Imperial Cancer Research
                    Fund, London, UK.
SOURCE:             Journal of molecular medicine (Berlin, Germany), (1998
                    May) Vol. 76, No. 6, pp. 421-33.  Ref: 70
                    Journal code: 9504370. ISSN: 0946-2716. L-ISSN: 0946-2716.
PUB. COUNTRY:       GERMANY: Germany, Federal Republic of
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199808
ENTRY DATE:         Entered STN: 20 Aug 1998
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                     Last Updated on STN: 20 Aug 1998
                     Entered Medline: 13 Aug 1998
REFERENCE COUNT:     70   There are 70 cited references for this document.
AB   The Hedgehog family of secreted glycoproteins proteins plays
     multifarious roles during vertebrate embryogenesis.  In both the
     Drosophila and vertebrate embryo correct deployment of Hedgehog
     -like proteins is critical for the generation of pattern in many tissues
     and organs.  New evidence now reveals that genes involved in
     hedgehog signalling are mutated in a number of common human
     genetic disorders, including skin cancer and craniofacial
     defects.  The understanding of how cells generate, receive and transduce
     the Hedgehog signal during development has led to the
     establishment of molecular paradigms for the pathogenesis of these
     diseases.  These studies clearly illustrate that knowledge of the normal
     role of a gene during development is critical for generating an
     understanding of the disease state in which it is mutated.

L20  ANSWER 23 OF 27     MEDLINE on STN
ACCESSION NUMBER:    1998103290     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 9440116
TITLE:               Expression of human GLI in mice results in failure to
                     thrive, early death, and patchy Hirschsprung-like
                     gastrointestinal dilatation.
AUTHOR:              Yang J T; Liu C Z; Villavicencio E H; Yoon J W; Walterhouse
                     D; Iannaccone P M
CORPORATE SOURCE:    Department of Pediatrics, Northwestern University Medical
                     School, Chicago, Illinois, USA.
CONTRACT NUMBER:     CA64395 (United States NCI NIH HHS)
                     HD28992 (United States NICHD NIH HHS)
SOURCE:              Molecular medicine (Cambridge, Mass.), (1997 Dec)
                     Vol. 3, No. 12, pp. 826-35.
                     Journal code: 9501023. ISSN: 1076-1551. L-ISSN: 1076-1551.
                     Report No.: NLM-PMC2230283.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
                     (RESEARCH SUPPORT, NON-U.S. GOV'T)
                     (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199802
ENTRY DATE:          Entered STN: 26 Feb 1998
                     Last Updated on STN: 26 Feb 1998
                     Entered Medline: 18 Feb 1998
MEDLINE REFERENCE COUNT:   29    There are 29 cited references available in
                                 MEDLINE for this document.
AB   BACKGROUND: GLI is an oncodevelopmental gene in the vertebrate
     hedgehog/patched signaling pathway that is spatiotemporally
     regulated during development and is amplified in a subset of human
     cancers.  GLI is the prototype for the Gli-Kruppel family of
     transcription factors, which includes the Drosophila segment polarity gene
     ci, the C. elegans sex-determining gene tra-1, and human and mouse GLI3,
     all of which contain a conserved domain of five C2-H2 zinc fingers.  GLI3
     mutations have been implicated in the mouse mutant extra toes, as well as
     in human Greig cephalopolydactaly syndrome and the autosomal dominant form
     of Pallister-Hall syndrome.  As such, GLI and the vertebrate
     hedgehog/patched signaling pathway appear to play important roles
     in both normal development and neoplasia.  MATERIALS AND METHODS: Since it
     is not known whether aberrant GLI expression is similarly linked to
     developmental disorders, we developed gain-of-function transgenic mice
     which express human GLI ectopically.  RESULTS: Affected transgenic mice
     exhibit a phenotype of failure to thrive, early death, and
     Hirschsprung-like patches of gastrointestinal dilatation.  The colons of
     affected mice have greatly attenuated smooth muscle layers and abnormal
     overlying epithelium.  The density of myenteric plexuses is reduced in the
     colonic walls.  The severity of the phenotype is related to the level of
     transgene expression.  CONCLUSIONS: The transgenic mouse model supports a
     role for GLI in gastrointestinal development.  As part of the vertebrate
     hedgehog/patched signaling pathway, GLI is essential to mesoderm
     and CNS ectoderm development and transgenic GLI expression affects
     neuronal, muscular, and epithelial cell differentiation in the
     gut.  Expression of human GLI in mice results in impairment of enteric
     neuronal development and a Hirschsprung-like phenotype.

L20  ANSWER 24 OF 27     MEDLINE on STN
ACCESSION NUMBER:    1998086756     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 9425597
TITLE:               Molecular basis of the nevoid basal cell carcinoma
                     syndrome.
AUTHOR:              Wicking C; Bale A E
CORPORATE SOURCE:    Centre for Molecular and Cellular Biology, University of
                     Queensland, St. Lucia, Australia.
SOURCE:              Current opinion in pediatrics, (1997 Dec) Vol. 9,
                     No. 6, pp. 630-5.  Ref: 69
                     Journal code: 9000850. ISSN: 1040-8703. L-ISSN: 1040-8703.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
                     General Review; (REVIEW)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199802
ENTRY DATE:          Entered STN: 26 Feb 1998
                     Last Updated on STN: 26 Feb 1998
                     Entered Medline: 17 Feb 1998
REFERENCE COUNT:     69   There are 69 cited references for this document.
AB   Many genes originally identified because of their role in embryonic
     development are also important in control of cell growth and
     differentiation postnatally.  Mutations in some of these genes
     have been shown to contribute to carcinogenesis.  The nevoid basal cell
     carcinoma syndrome is an autosomal dominant disorder that
     predisposes to basal cell carcinomas of the skin as well as
     widespread developmental defects.  The gene for this disorder, NBCCS, maps
     to chromosome 9q22.3, and loss of heterozygosity at this site in both
     sporadic and hereditary basal cell carcinomas suggests that it
     functions as a tumor suppressor.  NBCCS was positionally cloned
     and shown to be the human homologue of the Drosophila gene, patched.
     Drosophila patched is part of the hedgehog signaling pathway,
     important in determining embryonic patterning and cell fate in multiple
     structures of the developing embryo.  That mutations in human patched
     result in dysregulation of several genes known to play a role in both
     organogenesis and carcinogenesis may explain both the birth defects and
     the cancer predisposition seen in the nevoid basal cell
     carcinoma syndrome.

L20  ANSWER 25 OF 27     MEDLINE on STN
ACCESSION NUMBER:    1997404161     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 9262247
TITLE:               Developmental genes and cancer: role of patched in basal
                     cell carcinoma of the skin.
AUTHOR:              Gailani M R; Bale A E
CORPORATE SOURCE:    Department of Pediatrics, Yale University School of
                     Medicine, New Haven, CT 06520, USA.. mae_gailani@yale.edu
SOURCE:              Journal of the National Cancer Institute, (1997 Aug
                     6) Vol. 89, No. 15, pp. 1103-9.  Ref: 98
                     Journal code: 7503089. ISSN: 0027-8874. L-ISSN: 0027-8874.
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PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199708
ENTRY DATE:         Entered STN: 8 Sep 1997
                    Last Updated on STN: 8 Sep 1997
                    Entered Medline: 28 Aug 1997
REFERENCE COUNT:    98   There are 98 cited references for this document.
AB   Many genes originally identified because of their role in embryonic
     development are also important in postnatal control of cell growth and
     differentiation.  Mutations in some of these genes have been shown
     to cause cancer.  Basal cell carcinoma (BCC) of the
     skin is the most common cancer in humans.  More than 750000 new
     cases are diagnosed annually, and the incidence is rising.  BCCs are
     slow-growing, locally invasive tumors that rarely metastasize
     but can result in extensive morbidity through local recurrence and tissue
     destruction.  Epidemiologic studies suggest that sunlight (particularly
     UVB radiation) is a strong risk factor for BCC formation, although other
     factors are also involved.  The nevoid basal cell carcinoma
     syndrome (NBCCS), a rare genetic disorder, is characterized by
     predisposition to BCCs and other tumors as well as to a wide
     range of developmental defects.  NBCCS maps to chromosome 9q22.3, and loss
     of heterozygosity at this site in both sporadic and hereditary BCCs
     suggests that it functions as a tumor suppressor.  The gene for
     NBCCS was recently cloned and is the human homologue of the Drosophila
     gene "patched." Genetic studies in Drosophila show that patched is part of
     the hedgehog signaling pathway, which is important in
     determining embryonic patterning and cell fate in multiple structures of
     the developing embryo.  Human patched is mutated in both hereditary and
     sporadic BCCs, and inactivation of this gene is probably a necessary, if
     not sufficient, step for BCC formation.  Delineation of the biochemical
     pathway in which patched functions may lead to rational medical therapy
     for BCCs and possibly for other tumors associated with NBCCS.

L20  ANSWER 26 OF 27  EMBASE  COPYRIGHT (c) 2010 Elsevier B.V. All rights
     reserved on STN
ACCESSION NUMBER:   1998408628  EMBASE
TITLE:              Developmental genes and cancer: 'Patched' and basal cell
                    carcinoma of the skin.
AUTHOR:             Gailani, Mae (correspondence)
CORPORATE SOURCE:   Yale Child Health Research Center, Yale University School
                    of Medicine, 464 Congress Avenue, New Haven, CT 06520,
                    United States.
SOURCE:             Periodicum Biologorum, (Nov 1998) Vol. 100, No.
                    3, pp. 299-304.
                    Refs: 73
                    ISSN: 0031-5362  CODEN: PDBIAD
COUNTRY:            Croatia
DOCUMENT TYPE:      Journal; General Review; (Review)
FILE SEGMENT:       013     Dermatology and Venereology
                    016     Cancer
                    022     Human Genetics
                    029     Clinical and Experimental Biochemistry
LANGUAGE:           English
SUMMARY LANGUAGE:   English
ENTRY DATE:         Entered STN: 17 Dec 1998
                    Last Updated on STN: 17 Dec 1998
AB   Many genes originally identified because of their role in embryonic
     development are also important in post-natal control of cell growth and
     differentiation.  Mutations in some of these genes have been
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associated with various cancers. Basal cell carcinoma of the skin (BCC) is the most common cancer in humans. Over 750,000 new cases are diagnosed annually in the United States and the incidence is rising. BCCs are slow growing, locally invasive tumors that rarely metastasize but can result in extensive morbidity due to local recurrence and tissue destruction. Epidemiologic studies suggest that sunlight (particularly ultraviolet-B radiation) is a strong risk factor for BCC formation though other factors are also involved. A rare genetic disorder the nevoid basal cell carcinoma syndrome (NBCCS) is characterized by predisposition to BCCs and other tumors as well as a wide range of developmental defects. NBCCS maps to chromosome 9q22.3 and loss of heterozygosity at this site in both sporadic and hereditary BCCs suggests that it functions as a tumor suppressor. The gene for NBCCS was recently cloned and is the human homologue of the Drosophila segment polarity gene, 'patched'. Genetic studies in Drosophila show that patched is part of the hedgehog signalling pathway, important in determining embryonic patterning and cell fate in multiple structures of the developing larvae. Human patched is mutated in both hereditary and sporadic BCCs, and inactivation of this gene is probably a necessary if not sufficient step for BCC formation. Delineation of the biochemical pathway in which patched functions may lead to rational medical therapy for BCCs and possibly other tumors associated with NBCCS.

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ACCESSION NUMBER: 2001:547812 BIOSIS
DOCUMENT NUMBER: PREV200100547812
TITLE: Predicting temporal-spatial gene expression in neuronal progenitors using oligonucleotide microarrays.
AUTHOR(S): Zhao, Q. [Reprint author]; Kho, A.; Kenney, A. M. [Reprint author]; Yuk, D. [Reprint author]; Golub, T. R.; Kohane, I.; Zhang, Y. [Reprint author]; Rowitch, D. H. [Reprint author]
CORPORATE SOURCE: Pediatric Oncology, Dana-Farber Cancer Institute, Boston, MA, USA
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 1525. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience. San Diego, California, USA. November 10-15, 2001.
ISSN: 0190-5295.
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Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Nov 2001
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AB The genetic mechanisms regulating proliferation and differentiation of cerebellar granule neuron precursors (CGNP) during development are poorly understood. This issue is of particular interest because CGNP are thought to be the origin of the pediatric brain tumor, medulloblastoma. We have used Affymetrix Mu11K (GeneChips) oligonucleotide microarrays to identify genes upregulated in immature granule cells in primary cultures of post-natal day 5 (PN5) cerebellum when treated with the mitogen, Sonic Hedgehog (SHH). Despite such primary cultures are highly heterogeneous and contain only 15-20% proliferating cells, we observed a rapid upregulation (2-15 folds) of numerous genes when treated with SHH proteins. In contrast, we observed no significant increase in gene expression following growth arrest, suggesting that the granule cells in culture are relatively unresponsive to SHH upon cell cycle exit. Using novel analysis tools, we derived a list of genes/ESTs upregulated by Shh treatment and prospectively screened

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     their expression pattern by in situ hybridization, RT-PCR and northern
     blot.  This method accurately predicted gene expression specifically in
     the developing external granule cell layer of the PN7 cerebellum in 78% of
     cases tested.  These results demonstrate that appropriate in vitro models
     in conjunction with oligonucleotide microarrays may be used to accurately
     predict gene expression pattern and gene discovery in proliferating neural
     precursors.


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                S CYCLOPAMINE/CN

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L4            1 S JERVINE/CN

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L7          228 S JERVINE

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L17        3679 S HEDGEHOG/AB AND (CANCER OR TUMOR OR TUMOUR OR NEOPLASM OR CAR
L18         313 S L17 AND PD<20010702
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L20          27 S L19 AND (APOPTOSIS OR DIFFERENTIATION)

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